

REFERENCES

- Bonate PL (2000) *Analysis of Pretest-Posttest Designs*. Chapman & Hall/CRC: Boca Raton, Florida, USA
- Borm GF, Fransen J, Lemmens WAJG (2007) A simple sample size formula for analysis of covariance in randomized clinical trials. *J Clin Epidemiol* 60:1234–8
- Criscione VD, Weinstock MA, Naylor MF *et al.* (2009) Actinic keratoses natural history and risk of malignant transformation in the Veterans Affairs Topical Tretinoin Chemoprevention Trial. *Cancer* 115:2523–30
- Damian DL (2010) Photoprotective effects of nicotinamide (invited review). *Photochem Photobiol Sci* 9:578–85
- Damian DL, Patterson CRS, Stapelberg M *et al.* (2008) Ultraviolet radiation-induced immunosuppression is greater in men and prevented by topical nicotinamide. *J Invest Dermatol* 128:447–54
- Frost CA, Green AC (1994) Epidemiology of solar keratoses. *Br J Dermatol* 131:455–64
- Gensler HL, Williams T, Huang AC *et al.* (1999) Oral niacin prevents photocarcinogenesis and photoimmunosuppression in mice. *Nutr Cancer* 34:36–41
- Green A, Battistutta D (1990) Incidence and determinants of skin-cancer in a high-risk Australian population. *Int J Cancer* 46: 356–61
- Moloney FJ, Vestergaard ME, Radojkovic BL *et al.* (2010) Randomised, double-blinded, placebo controlled study to assess the effect of topical 1% nicotinamide on actinic keratoses. *Br J Dermatol* 162:1138–9
- Park J, Halliday GM, Surjana D *et al.* (2010) Nicotinamide prevents ultraviolet radiation-induced cellular energy loss. *Photochem Photobiol* 86:942–8
- Virag L, Szabo C (2002) The therapeutic potential of poly(ADP-ribose) polymerase inhibitors. *Pharmacol Rev* 54:375–429
- Yiasemides E, Sivapirabu G, Halliday GM *et al.* (2009) Oral nicotinamide protects against ultraviolet radiation-induced immunosuppression in humans. *Carcinogen* 30:101–5

Interpretation of Skindex-29 Scores: Response to Sampogna and Abeni

Journal of Investigative Dermatology (2012) **132**, 1500–1501; doi:10.1038/jid.2012.5; published online 16 February 2012

TO THE EDITOR

Until recently, little was known about the interpretability of scores of the Skindex-29, a well-established, dermatology-specific health-related quality of life (HRQoL) instrument (Chren *et al.*, 1997a,b). Nijsten *et al.* (2009) and Prinsen *et al.* (2010, 2011) were the first to identify the clinical meaningfulness of Skindex-29 scores by estimating a categorization of Skindex-29 scores, denoting mildly, moderately, and (very) severely impaired HRQoL (Nijsten *et al.*, 2009; Prinsen *et al.*, 2010, 2011).

In their thoughtful commentary in the *Journal of Investigative Dermatology*, 131, (9) September 2011, Sampogna and Abeni persuasively showed how different methods, a distribution-based and an anchor-based method, respectively, result in different categorizations of scores (Sampogna and Abeni, 2011). They applied the distribution-based ranges of scores found by Nijsten *et al.* and the anchor-based cutoff scores found by Prinsen *et al.* to an Italian sample of inpatients diagnosed with psoriasis, and to another Italian

sample of dermatological outpatients. By means of this comparison, differences between the two categorizations were shown; in general, the ranges of scores presented by Nijsten *et al.* were lower than the cutoff scores presented by Prinsen *et al.* Sampogna and Abeni also explored the clinical implications of these differences, for instance the consequence of using different categories in determining patient's eligibility for systemic treatment.

Unfortunately, a misinterpretation leading to an incorrect categorization

Table 1. An overview of the Skindex-29¹ cutoff scores derived by an anchor-based method (Prinsen *et al.*)² and the ranges of scores derived by a distribution-based method (Nijsten *et al.*)³

Categorization	Symptoms		Emotions		Functioning		Overall	
	Prinsen <i>et al.</i>	Nijsten <i>et al.</i>	Prinsen <i>et al.</i>	Nijsten <i>et al.</i>	Prinsen <i>et al.</i>	Nijsten <i>et al.</i>	Prinsen <i>et al.</i>	Nijsten <i>et al.</i>
Very little	—	<3	—	<5	—	<3	—	<5
Mild	≥39	4–10	≥24	6–24	≥21	4–10	≥25	6–17
Moderate	≥42	11–25	≥35	25–49	≥32	11–32	≥32	18–36
Severe	≥52	26–49	≥39	>50	≥37	>33	≥44	>37
Very severe	—	>50	—	—	—	—	—	—

¹The domain scores and the overall score are expressed on a 100-point scale, with higher scores indicating a lower level of quality of life.

²Skindex-29 cutoff scores are derived from the original articles (Prinsen *et al.*, 2010, 2011).

³Categorization of Skindex-29 scores are derived from the original article (Nijsten *et al.*, 2009).

Abbreviations: HRQoL, health-related quality of life

of scores was made. To illustrate, according to Prinsen *et al.*, the cutoff scores for mildly, moderately, and severely impaired HRQoL on the emotions domain were ≥ 24 , ≥ 35 , and ≥ 39 , respectively, meaning that a patient with a score ≥ 24 can be categorized as having a mildly impaired HRQoL on this domain, a score ≥ 35 as “moderate”, etc. However, Sampogna and Abeni categorized “mild” as having a score between 0 and 23.9 and, as a consequence, misclassified all cutoff scores. Therefore, we would like to provide a correct overview of the categorization of Skindex-29 scores (Table 1).

Having said this, we fully agree with Sampogna and Abeni on the limitations of both methods, such as dependence on the distribution of HRQoL scores in estimation samples and biases when using prospective anchors. Nevertheless, we believe that, under the condition that the same scale or anchor question is being used, anchor-based methods may lead to less variant estimates of cutoff scores than distribution-based methods. In addition, anchor-based methods are less dependent on the sociocultural and clinical characteristics of the estimation sample. For example, patients in one sample, scoring themselves as having a severely impaired HRQoL on a global rating scale or anchor question (for instance, an anchor question such as “In your opinion, how severe is your skin con-

dition?”), are likely to have Skindex-29 scores in the same range of scores as patients of another sample who also score themselves as having a severely impaired HRQoL. Nevertheless, the phrasing of an anchor question is a great source of variation in the comparison of different cutoff scores. We therefore advocate the use of standardized anchors.

A clinically meaningful interpretation of Skindex-29 scores is of great value. At present, two studies on this intriguing subject are available. As already expressed by Sampogna and Abeni, the combination of an anchor-based and a distribution-based method in a subsequent study would allow an objective comparison of the results within one study population. In addition to this, we recommend including standardized anchors, and to conduct such a study on an international level. Eventually, such efforts will contribute to reaching consensus on the categorization of scores so that they can be applied in clinical practice.

CONFLICT OF INTEREST

The authors state no conflict of interest.

ACKNOWLEDGMENTS

We thank MAG Sprangers (Academic Medical Center, University of Amsterdam, Department of Medical Psychology) and Phl Spuls (Academic Medical Center, University of Amsterdam, Department of Dermatology) for critically reviewing this letter.

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REFERENCES

- Chren MM, Lasek RJ, Flocke SA *et al.* (1997a) Improved discriminative and evaluative capability of a refined version of Skindex, a quality-of-life instrument for patients with skin diseases. *Arch Dermatol* 133:1433–40
- Chren MM, Lasek RJ, Quinn LM *et al.* (1997b) Convergent and discriminant validity of a generic and a disease-specific instrument to measure quality of life in patients with skin disease. *J Invest Dermatol* 108:103–7
- Nijsten T, Sampogna F, Abeni D (2009) Categorization of Skindex-29 scores using mixture analysis. *Dermatology* 218:151–4
- Prinsen CA, Lindeboom R, Sprangers MA *et al.* (2010) Health-related quality of life assessment in dermatology: interpretation of Skindex-29 scores using patient-based anchors. *J Invest Dermatol* 130:1318–22
- Prinsen CA, Lindeboom R, de Korte J (2011) Interpretation of Skindex-29 scores: cutoffs for mild, moderate, and severe impairment of health-related quality of life. *J Invest Dermatol* 131:1945–7
- Sampogna F, Abeni D (2011) Interpretation of Skindex-29 scores. *J Invest Dermatol* 131:1790–2

Application of an Indoleamine 2,3-Dioxygenase–Expressing Skin Substitute Improves Scar Formation in a Fibrotic Animal Model

Journal of Investigative Dermatology (2012) **132**, 1501–1505; doi:10.1038/jid.2011.467; published online 2 February 2012

TO THE EDITOR

Any delay in wound closure increases the probability of developing dermal fibrotic conditions such as hypertrophic

scars (Deitch *et al.*, 1983). For patients with extensive burn injuries, one of the most promising approaches is the application of an engineered skin sub-

stitute containing both epidermal and dermal cells (Coulomb *et al.*, 1998). Where allogeneic skin substitutes can provide a rapid, patient-ready wound coverage, they are susceptible to immune rejection. Our approach has been to engineer an allogeneic skin substitute